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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/500,180	03/23/2005	Peng Liu	514572002400	5337

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EXAMINER	
KAFIMOSAVI, HOSEIN	
ART UNIT	**PAPER NUMBER**
1795	

NOTIFICATION DATE	DELIVERY MODE
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

Office Action Summary	Application No.	Applicant(s)	
	10/500,180	LIU ET AL.	
	Examiner	Art Unit	
	HOSEIN KAFIMOSAVI	4132	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1 and 3-8* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1 and 3-8* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAIL ACTION

1. The amendment filed May 20, 2008 has been entered. Claims 1 and 3-7 remain pending in the application while claim 2 is cancelled and new claim 8 is added. Due to applicant's amendments, the previous 35 USC 102 and 35 USC 103 rejections of claims 1-7 are withdrawn and new grounds of rejection for claims 1 and 3-8 is presented below.

Claim Rejections - 35 USC § 102

2. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

3. Claim 1, 3, and 6-8 are rejected under 35 U.S.C. 102(e) as being anticipated by Zhao et al (US 6,939,451 B2).

As to claim 1, Zhao discloses a capillary electrophoresis chip apparatus (10) (capable of detecting nucleotide polymorphism or single nucleotide polymorphism)

(Col.14, 34-43) that comprises: an upper channel layer (18), comprising a two-dimensional or multidimensional microfluidic channel (14) (Fig. 1; Col. 5, lines 55 - 57; Col. 6; lines 24-25; Col. 15, lines 57-60; also US 5,599,432 incorporated by reference). Furthermore, Zhao discloses that the apparatus is assembled with the upper layer comprising channels that would connect the reservoirs in Figure 1 and therefore allowing a two-dimensional chip to be manufactured (Column 15, lines 57-60). Zhao also discloses an electrode aperture (24) (Col.5, 55-58) (for loading a sample), a middle electrode layer (20) capable of sealing the microfluid channel to form an intact capillary; said middle electrode layer comprising electrodes (capable of providing a needed voltage for the electrophoresis chip) (Col.5, 55-64; Col. 12, 28-34); and a lower heating layer (301) (capable of providing a table temperature gradient for electrophoresis), said lower heating layer comprising two or more sets of temperature control elements that are spaced apart from each other (Fig. 7C and Col. 13, 44-49), wherein the upper channel layer, the middle layer, the middle electrode layer, and the lower heating layer are thermal conductive and adhesive to each other (Col. 12, 21-23).

As to claim 3, Zhao discloses the capillary electrophoresis chip apparatus above, wherein the width, depth or diameter of the microchannels being between 1 to 200 □m (Col.6, 2-5) and a separation length of 18.5 cm (Col.15, 12-13).

As to claim 6, Zhao discloses the capillary electrophoresis chip apparatus above, wherein each temperature control element would be capable of being kept at a different constant temperature (so as to form a spatial temperature gradient) (Fig. 7C; Col. 13, lines 44-49; Col. 20, lines 30-31).

As to claim 7, Zhao discloses the capillary electrophoresis chip apparatus above, wherein the stable temperature gradient is capable of being a temporal temperature gradient (established by gradually and uniformly heating the whole chip) (Fig. 7C; Col. 13, lines 44-49; Col. 20, lines 30-31).

As to claim 8, Zhao discloses the capillary electrophoresis chip apparatus above, wherein the upper channel layer comprise a two-dimensional microfluid channel (Fig. 1; Col. 5, lines 55 - 57; Col. 6; lines 24-25; Col. 15, lines 57-60; also US 5,599,432 incorporated by reference), and the lower heating layer comprises two sets of temperature control elements that are spaced apart from each other, wherein each temperature control element is kept at a different constant temperature (so as to form a spatial temperature gradient) (Fig. 7C and Col. 13, 44-49, Col. 20, lines 30-31).

Claim Rejections - 35 USC § 103

4. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

5. The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

6. Claims 1, 3 and 6-8 are rejected under 35 U.S.C. 103(a) as being unpatentable over Zhao et al. (US 6,939,451 B2) in view of Kaltenbach et al (EP 0,770,871 A3, listed in IDS).

As to claim 1, the Examiner took the position that the heating layer (301) of Zhao would be capable of providing a stable temperature gradient. However, if it is not taken that the heating layer of Zhao would be capable of providing a stable temperature gradient; the following rejection is set forth to expedite prosecution.

Zhao discloses a bottom heating layer (301) to heat the chip (Fig. 7C) where the heating layer may comprise heaters placed within certain localized regions along the microchannels (Col. 13, lines 44-49).

Kaltenbach discloses a capillary electrophoresis chip comprising a miniaturized column device and a lower heating layer comprising heating elements (146 c, d and e; Fig. 10). The heating elements are in thermal contact with the middle layer and can be independently set to different temperatures thereby producing a spatial and temporal temperature gradient across the middle layer for increasing sample processing efficiency (Col. 25, lines 7-14 and 36-39 and 45-49).

It would have been obvious to one with ordinary skill in the art at the time of the invention to have the heaters comprising the lower heating layer of Zhao be independently set to different temperatures to produce a stable and temporal temperature gradient, as taught by Kaltenbach, a temperature gradient can improve the microfluidic chip by increasing sample processing and detection efficiency.

As to claim 3, Zhao in view of Kaltenbach, discloses the capillary electrophoresis chip apparatus above, wherein the width, depth or diameter of the microchannels being between 1 to 200 □m (Zhao at Col.6, 2-5) and a separation length of 18.5 cm (Zhao at Col.15, 12-13).

As to claim 6, Zhao in view of Kaltenbach, discloses the capillary electrophoresis chip apparatus above, wherein each temperature control element would be capable of being kept at a different constant temperature (so as to form a spatial temperature gradient) (Kaltenbach at Col. 25, lines 7-14 and 36-39 and 45-49).

As to claim 7, Zhao in view of Kaltenbach, discloses the capillary electrophoresis chip apparatus above, wherein the stable temperature gradient is capable of being a temporal temperature gradient (established by gradually and uniformly heating the whole chip) (Kaltenbach at Col. 25, lines 7-14 and 36-39 and 45-49).

As to claim 8, Zhao in further view of Kaltenbach, discloses the capillary electrophoresis chip apparatus above, wherein the upper channel layer comprise a two-dimensional microfluid channel (Zhao at Fig. 1; Col. 5, lines 55 - 57; Col. 6; lines 24-25; Col. 15, lines 57-60; also US 5,599,432 incorporated by reference), and the lower heating layer comprises two sets of temperature control elements that are spaced apart

from each other, wherein each temperature control element is kept at a different constant temperature (so as to form a spatial temperature gradient) (Kaltenbach at Col. 25, lines 7-14 and 36-39 and 45-49).

7. Claim 4 is rejected under 35 U.S.C. 103(a) as being unpatentable over Zhao et al (US 6,939,451 B2), or alternatively Zhao in view of Kaltenbach, as applied to claim 1 above, and further in view of Harvey A. Hodes (US 3,502,558).

As to claim 4, Zhao further discloses that the specific design and composition of the driving electrodes on the middle cover layer should be understood by those skilled in the art to be electrically conductive.

Zhao does not disclose the specific examples used in electrodes that are electrically conductive.

Harvey discloses a method of depositing gelatin on electrodes made of electrically conductive material such as gold, platinum or graphite (Col. 1, lines 62-67).

It would have been obvious to one with ordinary skill in the art at the time of the invention to have the middle electrode layer made of electrically conductive material such as gold, platinum or graphite, as taught by Harvey, in the invention of Zhao because Zhao already provides electrodes and as taught by Harvey the suitable electrode material can be any of gold, platinum or graphite because they are electrically conductive (Col.1, 62-67).

8. Claim 5 is rejected under 35 U.S.C. 103(a) as being unpatentable over Zhao et al. (US 6,939,451 B2), or alternatively Zhao in view of Kaltenbach, as applied to claim 1 above, and further in view of Johnck et al (US 2003/0161572 A1).

As to claim 5, Zhao further discloses that the middle cover layer can be coated with a pressure sensitive adhesive which is then pressed against the substrate containing channels and wells.

Zhao does not disclose the specific examples of pressure sensitive adhesives that can be used to coat the middle cover layer.

Johnck discloses a microfluidic analysis system consisting of an upper substrate layer and a middle cover layer with thin-film electrodes integrated thereon. Furthermore, Johnck discloses that the cover can be coated with polydimethylsiloxane (PDMS) which will be electrically insulating the exposed electrodes [0058].

It would have been obvious to one with ordinary skill in the art at the time of the invention to have the middle electrode layer (Col.12, lines 28-34) that bonds to the bottom of the substrate enclosing and sealing the microchannels and providing the voltage for electrophoresis to be coated where the pressure sensitive adhesive coating of the middle cover layer can be switched to a coating of polydimethylsiloxane (PDMS), as taught by Johnck, in the invention of Zhao because Zhao already provides a coating layer for the cover layer and as taught by Harvey the polydimethylsiloxane (PDMS) coating can electrically insulate the electrodes [0058].

Response to Arguments

9. Applicant's arguments filed May 20, 2008 have been fully considered but they are not persuasive.

Applicant argues on page 5 and 6 of the Remarks that Zhao does not teach a microfluidic chip for detecting a nucleotide polymorphism or a single nucleotide polymorphism and that it would be unable to resolve DNA fragments of the specific size with one or more base pair mismatches. Furthermore Applicant argues that Zhao does not teach two-dimensional or multidimensional microchannels on the microfluidic chip and the reference at Fig. 1 shows the microchannel (14) connecting only the two horizontal electrodes (28) and there is no evidence in the specification for the purpose of the vertical apertures containing electrodes. Applicant also argues that Zhao does not teach the idea of using heating elements to establish a stable thermal gradient and only teaches using the heating elements to "control the temperature" of the microchannel of the microfluidic chip.

In response to applicant's argument of using the microfluidic chip for detecting a nucleotide polymorphism or a single nucleotide polymorphism and using the heating elements to establish a thermal gradient, the examiner argues that a recitation of the intended use of the claimed invention must result in a structural difference between the claimed invention and the prior art in order to patentably distinguish the claimed invention from the prior art. If the prior art structure is capable of performing the intended use, then it meets the claim.

As to the argument that Zhao does not teach two-dimensional or multidimensional microchannels in the upper channel layer, Zhao discloses that the apparatus is assembled with the upper layer comprising channels that can connect the reservoirs in Figure 1 and therefore it would be inherent for the vertical reservoirs to

also be connected by a microchannel which would make the upper layer comprise of a two-dimensional microchannel. Furthermore, Zhao disclose that although it is not shown in the drawings, the upper channel layer may include one or more microchannels interconnected together which would teach a two-dimensional or multidimensional microchannel layer (Col. 15, lines 57-60; Col. 6, lines 24-25).

Applicant argues on page 8 - 11 of the Remarks that Zhao in view of cited reference, alone or in combination, does not teach a microfluidic chip for detecting a nucleotide polymorphism or a single nucleotide polymorphism and that it would be unable to resolve DNA fragments of the specific size with one or more base pair mismatches. Furthermore Applicant argues that Zhao in view of cited reference, alone or in combination, does not teach two-dimensional or multidimensional microchannels on the microfluidic chip. Applicant also argues that Zhao in view of cited reference, alone or in combination, does not teach the idea of using heating elements to establish a stable thermal gradient.

In response to applicant's above arguments, the primary reference in view of cited reference, alone or in combination, does show the features as argued above. In response to applicant's arguments against the references individually, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.,* 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986).

Conclusion

10. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to HOSEIN KAFIMOSAVI whose telephone number is (571)270-5271. The examiner can normally be reached on Mon - Fri, 7:30 AM - 5:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Alexa Neckel can be reached on (571)272-1446. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/H. K./
Examiner, Art Unit 4132

/Alexa D. Neckel/

Supervisory Patent Examiner, Art Unit 1795